



## The 65th ASH Annual Meeting Abstracts

## ONLINE PUBLICATION ONLY

## 705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALY AVAILABLE THERAPIES

**Evaluation of the Impact of Tocilizumab Use in Recipients of CAR T Cells for Non-Hodgkin Lymphoma**

Giulio Cassanello, MD<sup>1,2</sup>, Efrat Luttwak, MD<sup>3</sup>, Sean M. Devlin, PhD<sup>4</sup>, Alejandro Luna De Abia, MD PhD<sup>1</sup>, Magdalena Corona, MD<sup>1</sup>, Ivan Landego, MD<sup>1</sup>, Allison Parascondola, MPH<sup>1</sup>, Amethyst Saldia, BS<sup>1</sup>, Ana Alarcon Tomas, MD<sup>5,1</sup>, Parastoo B. Dahi, MD<sup>1</sup>, Richard J. Lin, MD<sup>1</sup>, M. Lia Palomba, MD<sup>6</sup>, Jae H. Park, MD<sup>7</sup>, Gilles Salles, MD PhD<sup>6</sup>, Miguel-Angel Perales, MD<sup>1</sup>, Michael Scordo<sup>1</sup>, Roni Shouval, MD PhD<sup>1</sup>, Gunjan L. Shah<sup>1</sup>

<sup>1</sup>Adult Bone Marrow Transplant Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

<sup>2</sup>University of Milan, Milan, Italy

<sup>3</sup>Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

<sup>4</sup>Department of Biostatistics and Epidemiology, Memorial Sloan Kettering Cancer Center, New York, NY

<sup>5</sup>Division of Hematology and Hemotherapy, Hospital General Universitario Gregorio Maranon, Madrid, Spain

<sup>6</sup>Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York

<sup>7</sup>Memorial Sloan Kettering Cancer Center, New York, NY

**Introduction:** CAR T has revolutionized the treatment of patients with relapsed or refractory (R/R) Non-Hodgkin lymphoma (NHL). Treatment of the major toxicity of cytokine release syndrome (CRS) is tocilizumab (toci) and corticosteroids based on the ASTCT grade. Real-world experiences in the United States and Europe have reported a higher rate of tocilizumab use than in pivotal trials; however, the impact of single or multiple administrations on clinical outcomes is not clear.

**Methods:** Patients diagnosed with diffuse (DLBCL), high grade (HGBCL) and primary mediastinal B cell lymphoma (PMBL) treated at our institution with commercial CAR T were retrospectively identified. The association between the number of doses received with best overall response by day 100, PFS, and OS was investigated through a Cox regression model using a 14-day landmark analysis. Late neutropenia was defined as an ANC <1000/mmc for two consecutive counts beyond day 30 post CAR-T infusion and a 30-day landmark analysis was performed in this case.

**Results:** 230 patients with R/R DLBCL (80%), HGBCL (17%) and PMBL (3%) were included in the analysis. Axicabtagene ciloleucel (Axi-cel), tisagenlecleucel (Tisa-cel), and lisocabtagene maraleucel (Liso-cel) were administered in 62%, 29% and 9% of cases, respectively. Median age at time of CAR-T infusion was 65 years (range 20-86), with a male predominance (63%). The median number of prior treatment lines was 3 (range 1-12), and 21% underwent a prior autologous hematopoietic cell transplant. Disease burden prior to CAR-T infusion can be inferred by the following: bridging therapy was deemed necessary in 77% of patients, pre-lymphodepletion LDH was elevated in 40%, and bulky disease with largest mass diameter was > 10 cm in 10%. CRS and ICANS were grade 2 in 107 patients (46%) and 46 patients (20%), respectively. Median time to first administration of toci was 4 days (range 1-16) with patients receiving 0 (51%), 1 (27%), 2 (14%), or 3-4 (8%) doses. Best response by day 100 for the whole cohort was CR in 138 (60%) and PR in 36 (16%) patients. In univariable analysis, factors associated with a lower likelihood of response were the administration of Tisa-cel ( $p=0.014$ ), bulky disease ( $p<0.001$ ), administration of bridging therapy ( $p=0.009$ ), and being refractory to the last treatment line ( $p=0.006$ ). Number of doses of tocilizumab did not impact the likelihood of response ( $p=0.72$ ). In a Cox regression model for survival, number of doses of tocilizumab was not associated with worse PFS ( $p=0.38$ , Figure 1) or OS ( $p=0.64$ ), while other known negative predictors of response had impact on survival, such as bulky and refractory disease.

By univariable analysis, tocilizumab administration was significantly associated with prolonged neutropenia ( $p<0.001$ ). The likelihood to observe an ANC<1000/mmc beyond day 30 increased accordingly to the number of doses received (Figure 2). Other factors associated with late neutropenia were bulky disease ( $P=0.013$ ), need of bridging therapy ( $p=0.004$ ), and corticosteroids administration ( $p<0.001$ ).

**Conclusion:** The number of tocilizumab infusions did not impact CAR T efficacy in terms of overall response and long-term survival, a finding that is concordant with other real-world experiences. The cumulative incidence of late neutropenia events was impacted by the number of doses received. We speculate that a severe CRS driven systemic inflammatory response, requiring several tocilizumab and corticosteroids administrations, may hinder the bone marrow function and recovery.

**Disclosures Palomba:** BMS: Honoraria; *Cellectar*: Honoraria; *Ceramedix*: Honoraria; *Juno*: Honoraria, Patents & Royalties; *Kite*: Honoraria; *MustangBio*: Honoraria; *GarudaTherapeutics*: Honoraria; *Novartis*: Honoraria; *Pluto Immunotherapeutics*: Honoraria; *Rheos*: Honoraria; *Seres Therapeutics*: Honoraria, Patents & Royalties; *Smart Immune*: Honoraria; *Thymofox*: Honoraria; *Synthekine*: Honoraria. **Park:** GC Cell: Membership on an entity's Board of Directors or advisory committees; *Incyte*: Research Funding; *Autolus Therapeutics*: Research Funding; *Fate Therapeutics*: Research Funding; *Allogene*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Servier*: Consultancy, Research Funding; *Intella*: Consultancy; *Takeda*: Consultancy, Research Funding; *Sobi*: Consultancy, Research Funding; *Pfizer*: Consultancy; *Minerva Bio*: Consultancy; *Kite*: Consultancy; *Curocell*: Consultancy; *Bright Pharmaceuticals*: Consultancy; *BeiGene*: Consultancy; *Be Biopharma*: Consultancy; *Amgen*: Consultancy; *Genentech, Inc.*: Research Funding; *Artiva Biotherapeutics*: Consultancy, Current holder of stock options in a privately-held company, Membership on an entity's Board of Directors or advisory committees; *Affyimmune*: Consultancy. **Salles:** *AbbVie*: Consultancy, Honoraria; *Merck*: Consultancy, Honoraria; *ATB Therapeutics*: Consultancy; *BMS/Celgene*: Consultancy; *Debiopharm*: Consultancy; *Genmab*: Consultancy; *Incyte*: Consultancy; *BeiGene*: Consultancy; *Genentech, Inc./F. Hoffmann-La Roche Ltd*: Consultancy, Research Funding; *Janssen*: Consultancy, Research Funding; *Kite/Gilead*: Consultancy; *Loxo/Lilly*: Consultancy; *Molecular Partners*: Consultancy; *Novartis*: Consultancy; *Nurix*: Consultancy; *Orna*: Consultancy; *Ipsen*: Consultancy, Research Funding; *Nordic Nanovector*: Consultancy; *Owkin*: Current holder of stock options in a privately-held company; *EPIZYME*: Consultancy. **Perales:** *Allogene*: Research Funding; *Astellas*: Consultancy, Honoraria; *Adicet*: Honoraria; *Incyte*: Consultancy, Honoraria, Research Funding; *Vor Biopharma*: Consultancy, Honoraria; *AbbVie*: Consultancy, Honoraria; *Omeros*: Consultancy, Current equity holder in publicly-traded company, Honoraria; *Orcabio*: Consultancy, Current equity holder in publicly-traded company, Honoraria; *Takeda*: Consultancy, Honoraria; *MorphoSys*: Consultancy, Honoraria; *Celgene*: Honoraria; *Nektar Therapeutics*: Consultancy, Honoraria, Research Funding; *Novartis*: Consultancy, Honoraria, Research Funding; *Caribou*: Consultancy, Honoraria; *Equillum*: Consultancy, Honoraria; *DSMB*: Other; *Servier*: Other; *NexImmune*: Consultancy, Current equity holder in publicly-traded company; *Medigene*: Consultancy, Other; *Cidara Therapeutics*: Consultancy, Other; *Syncopation*: Honoraria; *Miltenyi Biotec*: Consultancy, Honoraria, Research Funding; *Merck*: Consultancy, Honoraria; *Exevir*: Consultancy, Honoraria; *BMS*: Consultancy, Honoraria; *Miltenyi Biotec*: Honoraria; *Sellas Life Sciences*: Consultancy; *VectivBio AG*: Consultancy, Honoraria; *Karyopharm*: Consultancy, Honoraria; *Kite*: Consultancy, Honoraria, Research Funding; *Allovir*: Consultancy. **Scordo:** *CancertNetwork (Intellisphere LLC)*: Honoraria; *Medscape, LLC*: Honoraria; *Omeros Corporation*: Consultancy, Research Funding; *Amgen, Inc.*: Research Funding; *Angiocrine Bioscience, Inc.*: Research Funding. **Shah:** *Amgen*: Research Funding; *BMS*: Research Funding; *ArcellX*: Other; *DSMB*; *Beyond Spring*: Research Funding; *Janssen*: Research Funding.

<https://doi.org/10.1182/blood-2023-190500>

Figure 2:

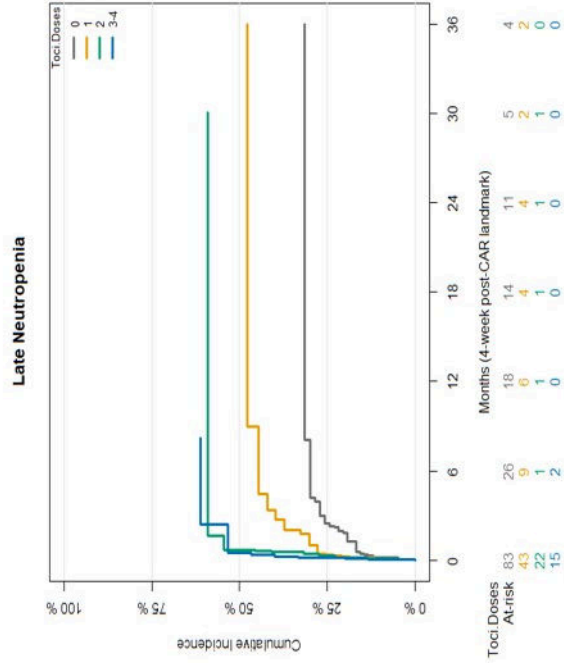


Figure 1:

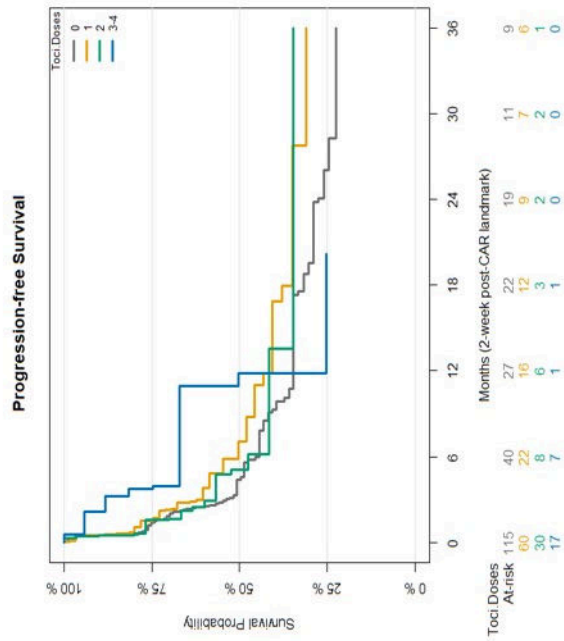


Figure 1